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AMENDMENTS TO THE CLAIMS

The Claim Listing below will replace all prior versions of the claims in the application:

1. (Currently amended) An isolated nucleic acid compound comprising at least a portion that is complementary to at least 15 contiguous nucleotides of an EphB4 transcript sequence set forth in SEQ ID NO: 392 and decreases the expression of EphB4 in a cell, wherein the nucleic acid compound is an antisense nucleic acid compound, and wherein the antisense nucleic acid compound comprises one or more modified backbone or base moieties, and wherein the modified antisense nucleic acid comprises at least one 2'-O-alkylated ribonucleotide.

2. (Canceled)

3. (Previously presented) The isolated nucleic acid compound of claim 1, wherein the nucleic acid compound comprises a nucleotide sequence that is complementary to a region consisting of no more than 500 nucleotides of the nucleic acid sequence as set forth in SEQ ID NO: 392.

4. (Canceled)

5. (Previously presented) The nucleic acid compound of claim 3, wherein the region is in the coding sequence of the sequence as set forth in SEQ ID NO: 392.

6. (Previously presented) The nucleic acid compound of claim 1, wherein nucleic acid compound is from about 15 to about 75 nucleotides in length.

7. (Original) The nucleic acid compound of claim 1, wherein the nucleic acid compound is single-stranded.

8. (Original) The nucleic acid compound of claim 1, wherein the nucleic acid compound is double-stranded.

9. (Original) The nucleic acid compound of claim 1, wherein the nucleic acid compound is a DNA molecule, optionally comprising one or more modified backbone or base moieties.

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10. (Original) The nucleic acid compound of claim 1, wherein the nucleic acid compound is a RNA molecule, optionally comprising one or more modified backbone or base moieties.

11. (Original) The nucleic acid compound of claim 1, wherein the nucleic acid compound comprises a DNA strand and a RNA strand and optionally comprises one or more modified backbone or base moieties.

12. (Canceled)

13. (Previously presented) The nucleic acid compound of claim 1, wherein the antisense nucleic acid compound is from about 15 to about 30 nucleotides in length.

14. (Previously presented) The nucleic acid compound of claim 3, wherein the antisense nucleic acid compound comprises a sequence selected from the sequences as forth in SEQ ID NOs: 73-232.

15. (Canceled)

16. (Currently amended) The nucleic acid compound of claim 1~~15~~, wherein the antisense nucleic acid compound has at least one internucleotide linkage selected from the group consisting of alkylphosphonates, phosphorothioates, phosphorodithioates, alkylphosphonothioates, phosphoramidates, phosphate esters, carbamates, acetamidate, carboxylmethyl esters, carbonates, and phosphate triesters.

17. (Canceled)

18. (Withdrawn) The nucleic acid compound of claim 1, wherein the nucleic acid compound is an RNAi construct.

19. (Withdrawn) The nucleic acid compound of claim 18, wherein the RNAi construct is a dsRNA, optionally comprising one or more modified backbone or base moieties.

20. (Withdrawn) The nucleic acid compound of claim 18, wherein the RNAi construct is a hairpin RNA, optionally comprising one or more modified backbone or base moieties.

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21. (Withdrawn) The nucleic acid compound of claim 18, wherein the duplex portion of the RNAi construct is from about 21 to about 23 nucleotides in length.

22. (Withdrawn) The nucleic acid compound of claim 18, wherein the RNAi construct comprises an RNA strand having a sequence selected from the sequences as forth in SEQ ID NOs: 233-290, optionally comprising one or more modified backbone or base moieties.

23. (Withdrawn) The nucleic acid compound of claim 18, wherein the RNAi construct comprises one or more backbone or base moieties.

24. (Withdrawn) The nucleic acid compound of claim 23, wherein the modified RNAi construct has at least one internucleotide linkage selected from the group consisting of alkylphosphonates, phosphorothioates, phosphorodithioates, alkylphosphonothioates, phosphoramidates, phosphate esters, carbamates, acetamidate, carboxylmethyl esters, carbonates, and phosphate triesters.

25. (Withdrawn) The nucleic acid compound of claim 24, wherein the modified RNAi construct comprises at least a 2'-O-alkylated ribonucleotide.

26-29. (Canceled)

30. (Withdrawn) An isolated nucleic acid compound comprising a portion that hybridizes to an EphrinB2 transcript under physiological conditions and decreases the expression of EphrinB2 in a cell.

31. (Withdrawn) The isolated nucleic acid compound of claim 30, wherein the EphrinB2 transcript has a nucleotide sequence shown in Figure 64.

32. (Withdrawn) The isolated nucleic acid compound of claim 30, wherein the nucleic acid compound comprises a nucleotide sequence that is complementary to a region consisting of no more than 500 nucleotides of the nucleic acid sequence shown in Figure 64.

33. (Withdrawn) The nucleic acid compound of claim 32, wherein the region has at least 8 contiguous nucleotides of the sequence shown in Figure 64.

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34. (Withdrawn) The nucleic acid compound of claim 32, wherein the region is in the coding sequence shown in Figure 64.

35. (Withdrawn) The nucleic acid compound of claim 30, wherein nucleic acid compound is from about 14 to about 50 nucleotides in length.

36. (Withdrawn) The nucleic acid compound of claim 30, wherein the nucleic acid compound is single-stranded.

37. (Withdrawn) The nucleic acid compound of claim 30, wherein the nucleic acid compound is double-stranded.

38. (Withdrawn) The nucleic acid compound of claim 30, wherein the nucleic acid compound is a DNA molecule, optionally comprising one or more modified backbone or base moieties.

39. (Withdrawn) The nucleic acid compound of claim 30, wherein the nucleic acid compound is a RNA molecule, optionally comprising one or more modified backbone or base moieties.

40. (Withdrawn) The nucleic acid compound of claim 30, wherein the nucleic acid compound comprises a DNA strand and a RNA strand and optionally comprises one or more modified backbone or base moieties.

41. (Withdrawn) The nucleic acid compound of claim 30, wherein the nucleic acid compound is an antisense nucleic acid compound.

42. (Withdrawn) The nucleic acid compound of claim 41, wherein the antisense nucleic acid compound is from about 15 to about 30 nucleotides in length.

43. (Withdrawn) The nucleic acid compound of claim 41, wherein the antisense nucleic acid compound is selected from the sequences listed in Table 8.

44. (Withdrawn) The nucleic acid compound of claim 41, wherein the antisense nucleic acid compound comprisese one or modified backbone or base moieties.

45. (Withdrawn) The nucleic acid compound of claim 44, wherein the antisense nucleic acid compound has at least one internucleotide linkage selected from the group consisting of

alkylphosphonates, phosphorothioates, phosphorodithioates, alkylphosphonothioates, phosphoramidates, phosphate esters, carbamates, acetamidate, carboxylmethyl esters, carbonates, and phosphate triesters.

46. (Withdrawn) The nucleic acid compound of claim 44, wherein the modified antisense nucleic acid comprises at least one 2'-O-alkylated ribonucleotide.

47. (Withdrawn) The nucleic acid compound of claim 30, wherein the nucleic acid compound is a RNAi construct.

48. (Withdrawn) The nucleic acid compound of claim 47, wherein the RNAi construct is a dsRNA, optionally comprising one or more modified backbone or base moieties.

49. (Withdrawn) The nucleic acid compound of claim 47, wherein the RNAi construct is a hairpin RNA, optionally comprising one or more modified backbone or base moieties.

50. (Withdrawn) The nucleic acid compound of claim 47, wherein the duplex portion of the RNAi construct is from about 21 to about 23 nucleotides in length.

51. (Withdrawn) The nucleic acid compound of claim 47, wherein the RNAi construct comprises an RNA strand having a sequence selected from the sequences listed in Table 9, optionally comprising one or more modified backbone or base moieties.

52. (Withdrawn) The nucleic acid compound of claim 47, wherein the RNAi construct comprises one or more backbone or base moieties.

53. (Withdrawn) The nucleic acid compound of claim 52, wherein the modified RNAi construct has at least one internucleotide linkage selected from the group consisting of alkylphosphonates, phosphorothioates, phosphorodithioates, alkylphosphonothioates, phosphoramidates, phosphate esters, carbamates, acetamidate, carboxylmethyl esters, carbonates, and phosphate triesters.

54. (Withdrawn) The nucleic acid compound of claim 52, wherein the modified RNAi construct comprises at least a 2'-O-alkylated ribonucleotide.

55. (Withdrawn) The nucleic acid compound of claim 30, wherein the nucleic acid compound is an enzymatic nucleic acid.

56. (Withdrawn) The nucleic acid compound of claim 55, wherein the enzymatic nucleic acid is a ribozyme.

57. (Withdrawn) The nucleic acid compound of claim 55, wherein the enzymatic nucleic acid is a DNA enzyme.

58. (Withdrawn) The nucleic acid compound of claim 30, wherein the nucleic acid compound inhibits EphrinB2 expression in cells by 50% or greater, when contacted with the cells under physiological conditions at a concentration of 5 micromolar.

59. (Currently amended) A pharmaceutical composition comprising a nucleic acid compound and a pharmaceutically acceptable carrier, wherein the nucleic acid compound is complementary to at least 15 contiguous nucleotides of an EphB4 transcript sequence set forth in SEQ ID NO: 392 and decreases the expression of EphB4 in a cell, wherein the nucleic acid compound is an antisense nucleic acid compound, and wherein the antisense nucleic acid compound comprises one or more modified backbone or base moieties, and wherein the modified antisense nucleic acid comprises at least one 2'-O-alkylated ribonucleotide.

60. (Canceled)

61. (Withdrawn) A method of inhibiting EphB4 expression in a cell, comprising contacting the cell with an effective amount of the nucleic acid compound of claim 1.

62. (Withdrawn) The method of claim 61, wherein the nucleic acid compound is selected from the group consisting of: an RNAi construct and an antisense nucleic acid compound.

63. (Withdrawn) A method of inhibiting Ephrin B2 expression in a cell, comprising contacting the cell with an effective amount of the nucleic acid compound of claim 30.

64. (Withdrawn) The method of claim 63, wherein the wherein the nucleic acid compound is selected from the group consisting of: an RNAi construct and an antisense nucleic acid compound.

65. (Withdrawn) A method of reducing the growth rate of a tumor in a subject, comprising administering an amount of a nucleic acid compound sufficient to reduce the growth rate of the tumor, wherein the nucleic acid compound is selected from the group consisting of:

(a) a nucleic acid compound that hybridizes to an EphB4 transcript under physiological conditions and decreases the expression of EphB4 in a cell; and

(b) a nucleic acid compound that hybridizes to an EphrinB2 transcript under physiological conditions and decreases the expression of EphrinB2 in a cell.

66. (Withdrawn) The method of claim 65, wherein the tumor comprises one or more cancer cells expressing EphB4 and/or EphrinB2.

67. (Withdrawn) A method for treating a patient suffering from a cancer, comprising administering to the patient a nucleic acid moclecule selected from the group consisting of:

(a) a nucleic acid compound that hybridizes to an EphB4 transcript under physiological conditions and decreases the expression of EphB4 in a cell; and

(b) a nucleic acid compound that hybridizes to an EphrinB2 transcript under physiological conditions and decreases the expression of EphrinB2 in a cell.

68. (Withdrawn) The method of claim 67, wherein the nucleic acid compound is an antisense nucleic acid compound.

69. (Withdrawn) The method of claim 67, wherein the nucleic acid compound is an RNAi construct.

70. (Withdrawn) The method of claim 67, wherein the nucleic acid compound is formulated with a pharmaceutically acceptable carrier.

71. (Withdrawn) The method of claim 67, wherein the cancer cell expresses a higher level of EphB4 compared to a noncancerous cell from a comparable tissue.

72. (Withdrawn) The method of claim 67, wherein the cancer cell expresses a higher level of Ephrin B2 compared to a noncancerous cell from a comparable tissue.

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73. (Withdrawn) The method of claim 67, wherein the tumor is a metastatic tumor.

74. (Withdrawn) The method of claim 67, wherein the tumor is seleted from the group consisting of colon carcinoma, breast tumor, mesothelioma, prostate tumor, squamous cell carcinoma, Kaposi sarcoma, and leukemia.

75. (Withdrawn) The method of claim 67, wherein the tumor is an angiogenesis-dependent tumor.

76. (Withdrawn) The method of claim 67, wherein the tumor is an angiogenesis-independent tumor.

77. (Withdrawn) The method of claim 67, further including at least one additional anti-cancer chemotherapeutic agent that inhibits cancer cells in an additive or synergistic manner with the nucleic acid compound.

78. (Withdrawn) A method for treating a patient suffering from an angiogenesis-associated disease, comprising administering to the patient an amount of a nucleic acid compound sufficient to inhibit angiogenesis, wherein the nucleic acid compound is selected from the group consisting of:

(a) a nucleic acid compound that hybridizes to an EphB4 transcript under physiological conditions and decreases the expression of EphB4 in a cell; and

(b) a nucleic acid compound that hybridizes to an EphrinB2 transcript under physiological conditions and decreases the expression of EphrinB2 in a cell.

79. (Withdrawn) The method of claim 78, wherein the nucleic acid compound is an antisense nucleic acid compound.

80. (Withdrawn) The method of claim 78, wherein the nucleic acid compound is an RNAi construct.

81. (Withdrawn) The method of claim 78, wherein the nucleic acid compound is formulated with a pharmaceutically acceptable carrier.

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82. (Withdrawn) The method of claim 78, wherein the angiogenesis-associated disease is selected from the group consisting of angiogenesis-dependent cancer, benign tumors, inflammatory disorders, chronic articular rheumatism and psoriasis, ocular angiogenic diseases, Osler-Webber Syndrome, myocardial angiogenesis, plaque neovascularization, telangiectasia, hemophiliac joints, angiofibroma, wound granulation, wound healing, telangiectasia psoriasis scleroderma, pyogenic granuloma, cororany collaterals, ischemic limb angiogenesis, rubeosis, arthritis, diabetic neovascularization, fractures, vasculogenesis, and hematopoiesis.

83. (Withdrawn) The method of claim 78, further including at least one additional anti-angiogenesis agent that inhibits angiogenesis in an additive or synergistic manner with the nucleic acid compound.

84-87. (Canceled)

88. (Withdrawn) A method for treating a patient suffering from a cancer, comprising:

(a) identifying in the patient a tumor having a plurality of cancer cells that express EphB4 and/or EphrinB2; and

(b) administering to the patient a nucleic acid compound selected from the group consisting of:

(i) a nucleic acid compound that hybridizes to an EphB4 transcript under physiological conditions and decreases the expression of EphB4 in a cell; and

(ii) a nucleic acid compound that hybridizes to an EphrinB2 transcript under physiological conditions and decreases the expression of EphrinB2 in a cell.

89. (Withdrawn) A method for treating a patient suffering from a cancer, comprising:

(a) identifying in the patient a tumor having a plurality of cancer cells having a gene amplification of the EphB4 and/or EphrinB2 gene; and

(b) administering to the patient a nucleic acid compound selected from the group consisting of:

(i) a nucleic acid compound that hybridizes to an EphB4 transcript under physiological conditions and decreases the expression of EphB4 in a cell; and

(ii) a nucleic acid compound that hybridizes to an EphrinB2 transcript under physiological conditions and decreases the expression of EphrinB2 in a cell.

90. (Withdrawn) A method for identifying a tumor that is suitable for treatment with an inhibitor of EphrinB2 or EphB4 expression, the method comprising detecting in the tumor cell one or more of the following characteristics:

(a) expression of EphB4 protein and/or mRNA;

(b) expression of EphrinB2 protein and/or mRNA;

(c) gene amplification of the EphB4 gene; and

(d) gene amplification of the EphrinB2 gene,

wherein a tumor cell having one or more of characteristics (a)-(d) is suitable for treatment with an inhibitor of EphrinB2 or EphB4 expression.

91. (Withdrawn) The method of claim 60, wherein the inhibitor of EphrinB2 or EphB4 expression is selected from the group consisting of:

(i) a nucleic acid compound that hybridizes to an EphB4 transcript under physiological conditions and decreases the expression of EphB4 in a cell; and

(ii) a nucleic acid compound that hybridizes to an EphrinB2 transcript under physiological conditions and decreases the expression of EphrinB2 in a cell.

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